

Figure 1. Structures of Monocillin I, Radicicol and Geldanamycin

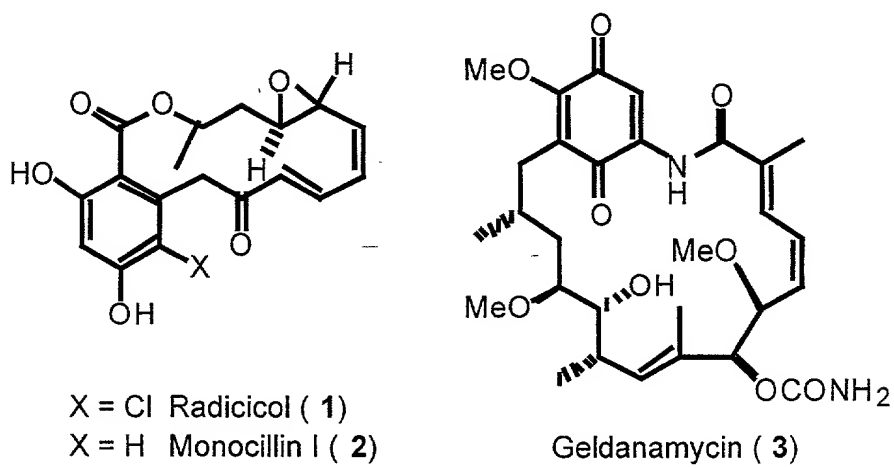


Figure 1

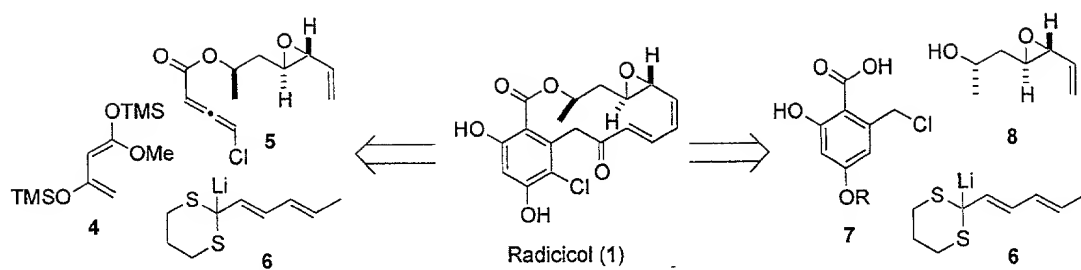
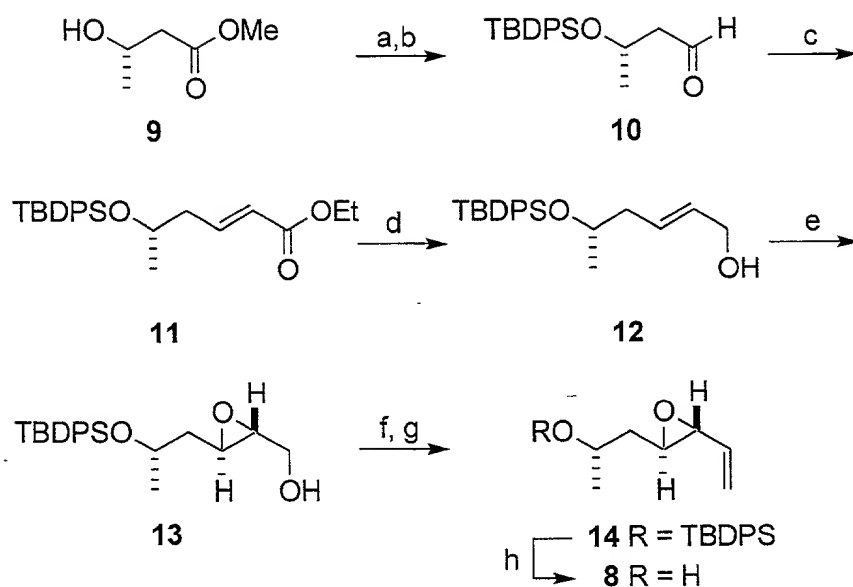


Figure 2

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(a) TBDPSCl, imid., >95%; (b) DIBAL-H, -78 °C, 92%; (c) LiCl, DIPEA (EtO)₂P(O)CH₂CO₂Et, 95%;
 (d) DIBAL-H, -20 °C, 96%; (e) (+)-DET, Ti(O*i*Pr)₄, TBHP, 90%, >95% ee; (f) SO₃·pyridine, Et₃N, DMSO, 90%;
 (g) Ph₃PCH₃Br, NaHMDS, 0 °C, 82%; (h) TBAF, 89%.

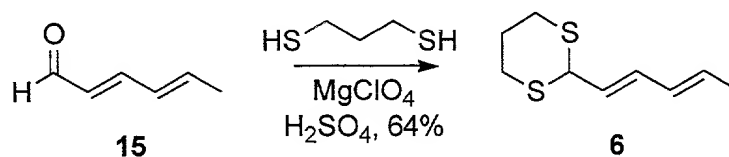
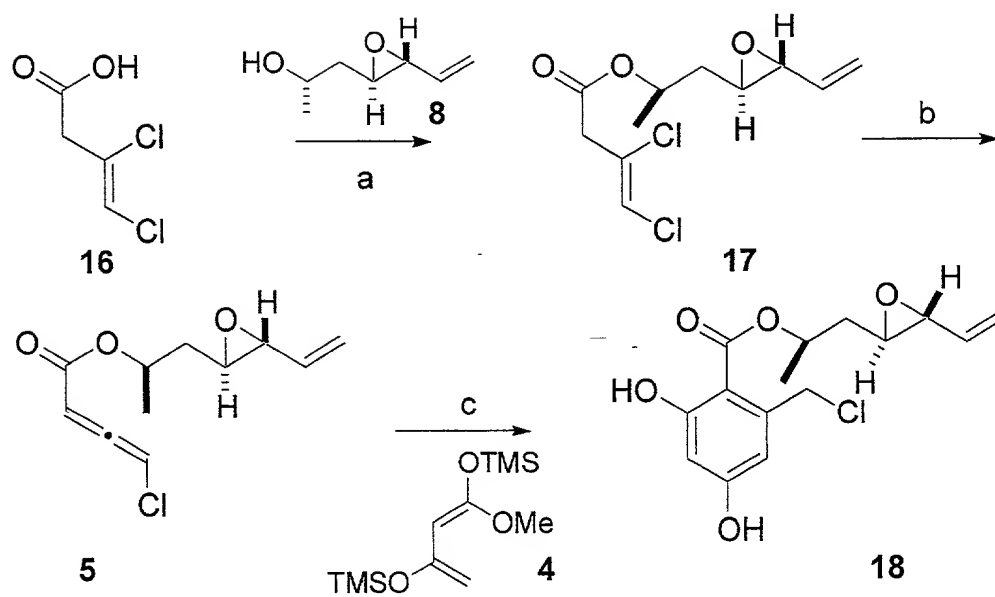


Figure 3

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a. DEAD, PPh_3 , 70%; b. iPr_2NEt , 70%; c. 50% (4:1)

Figure 4

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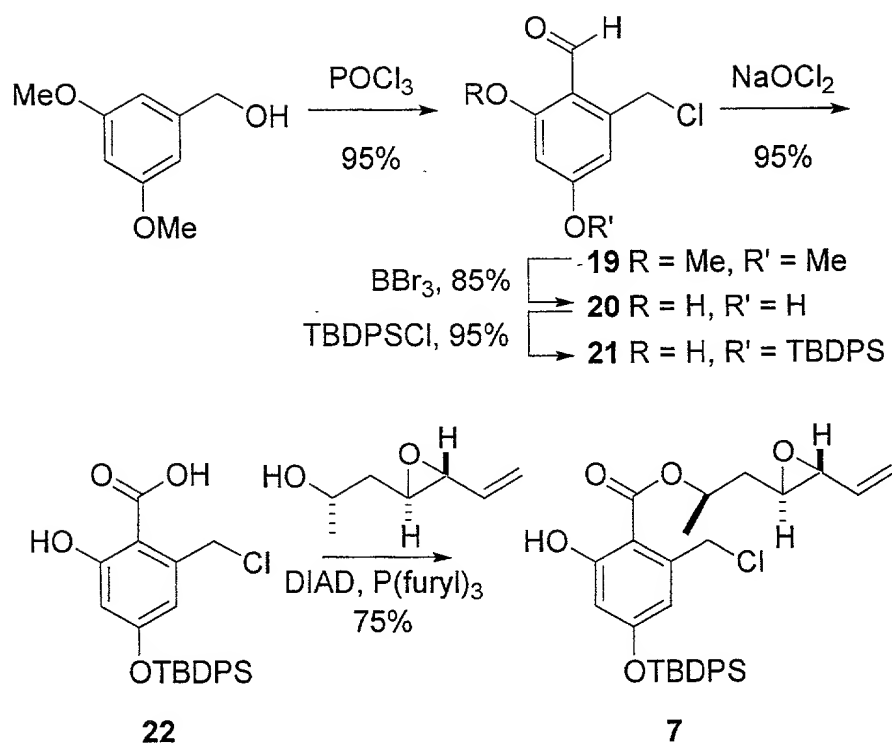
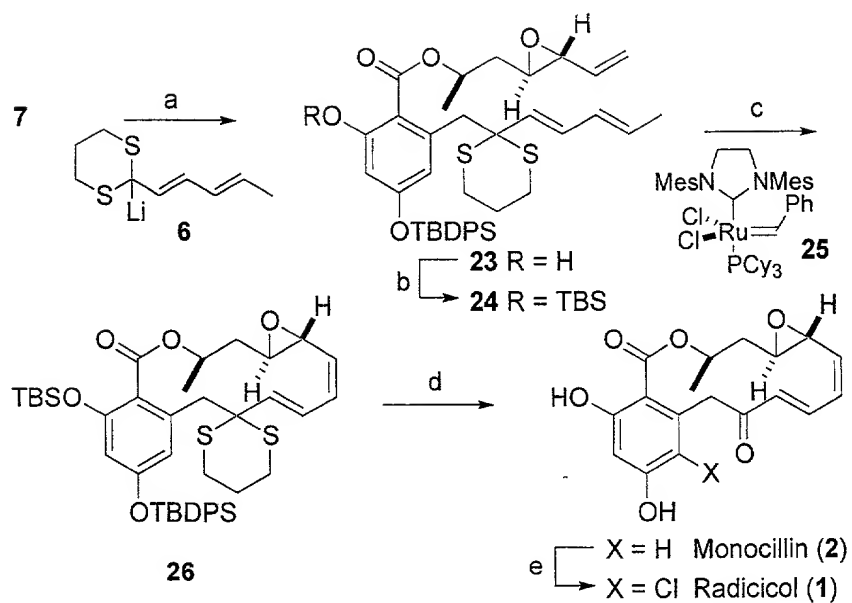


Figure 5

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a. *n*-BuLi, -78°C , 50% (6:1); b. TBSCl, 83%; c. 42°C , 70%; d. (i) mCPBA, (ii) Ac₂O, Et₃N, H₂O, 60°C , (iii) NaHCO₃, MeOH, 60%; e. SO₂Cl₂, 50%

Figure 6

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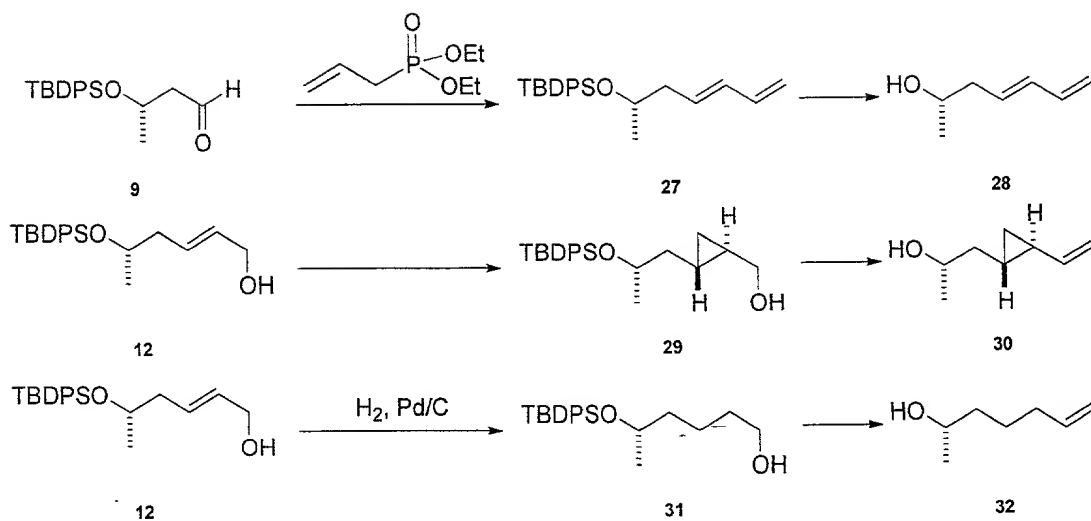


Figure 7

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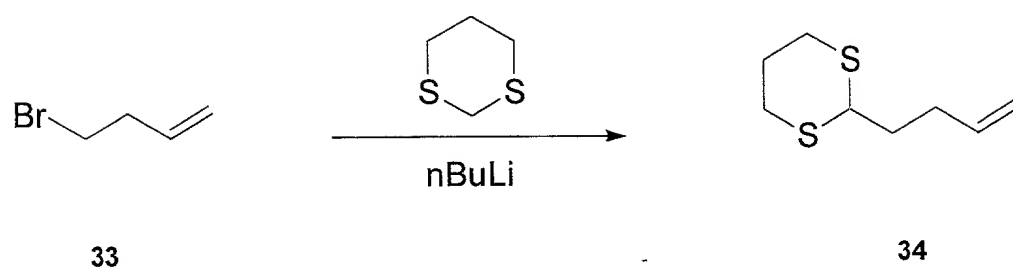


Figure 8

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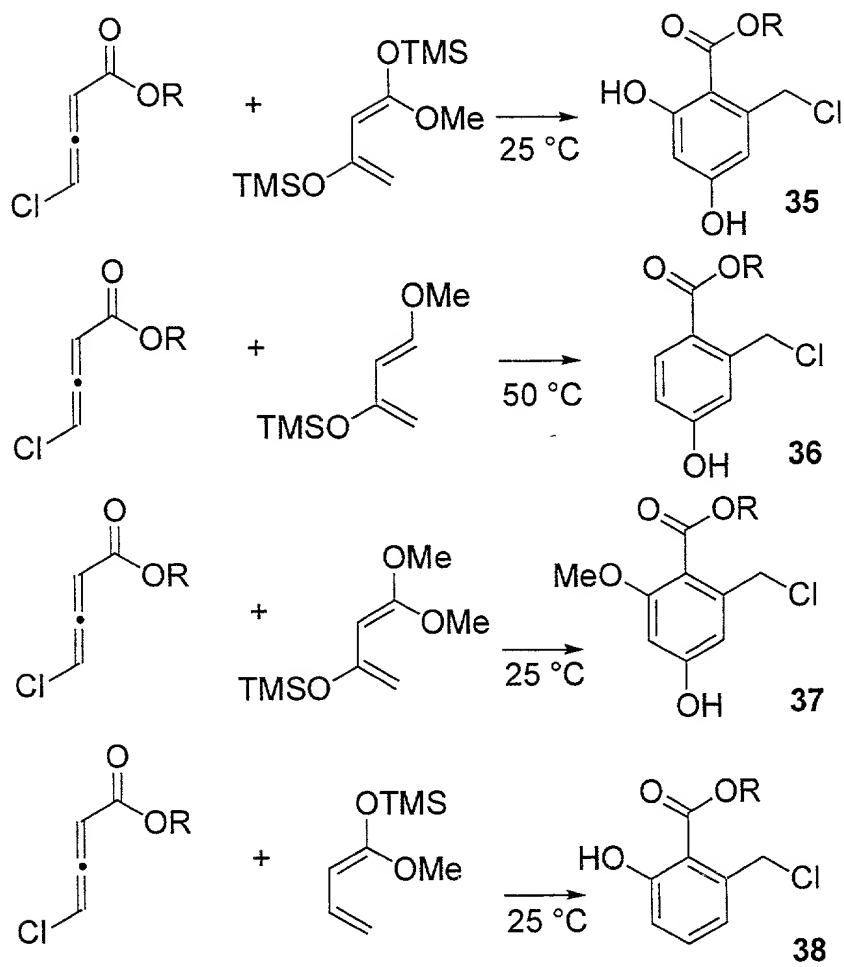


Figure 9

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Generation of Diversity at Aromatic Positions

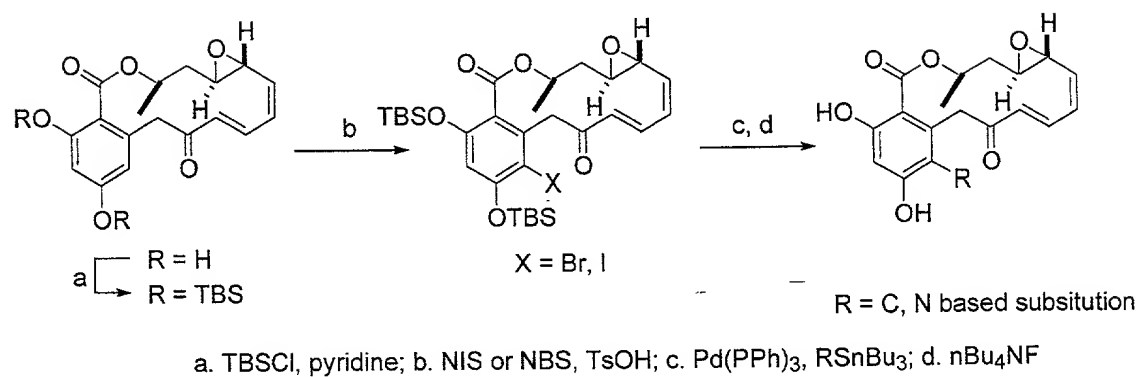


Figure 10

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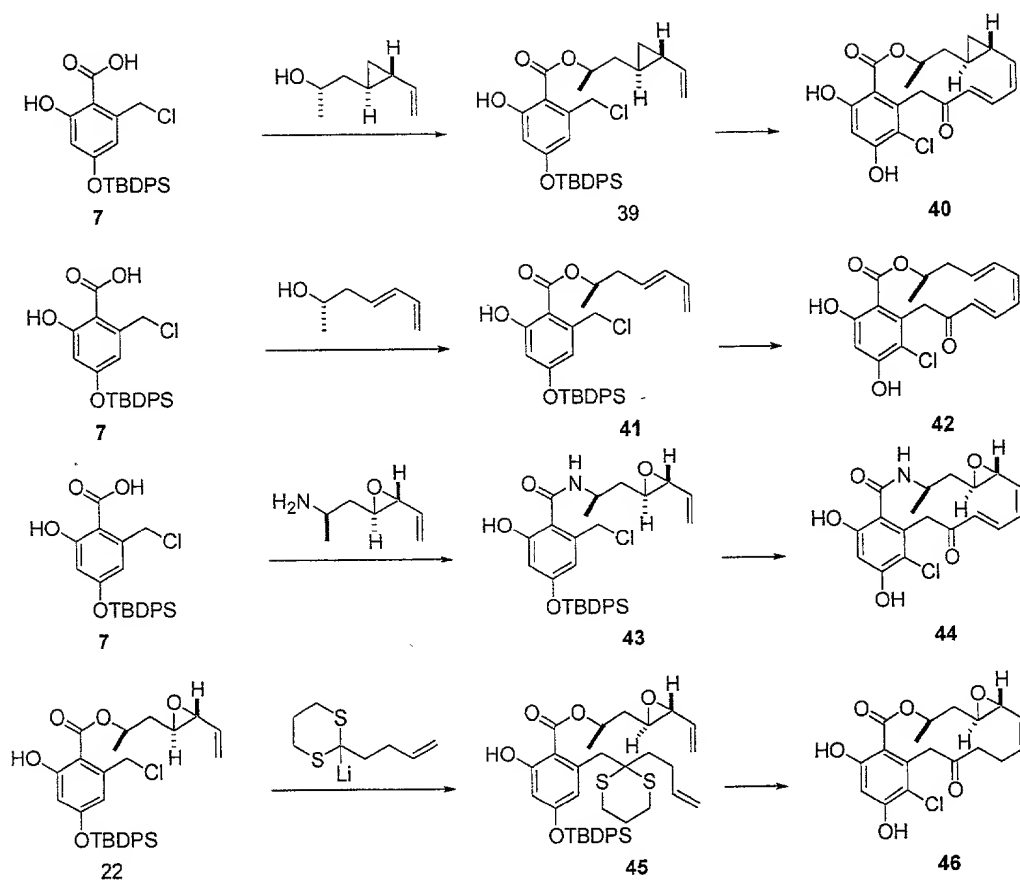


Figure 11

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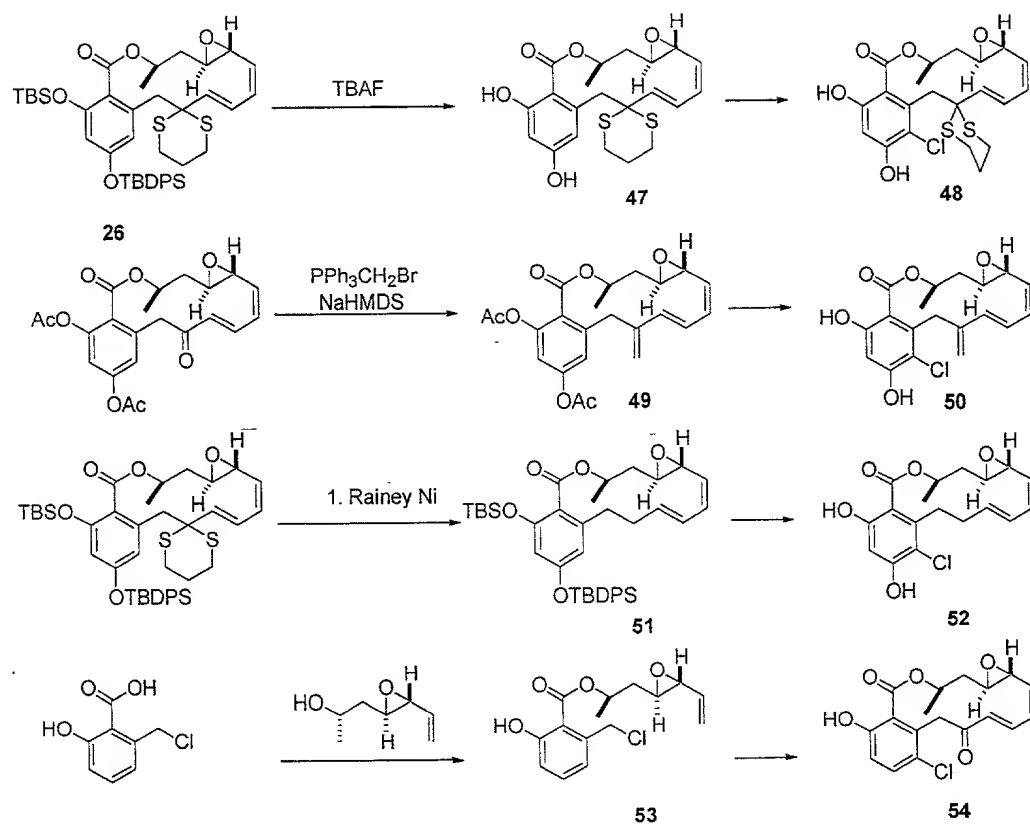
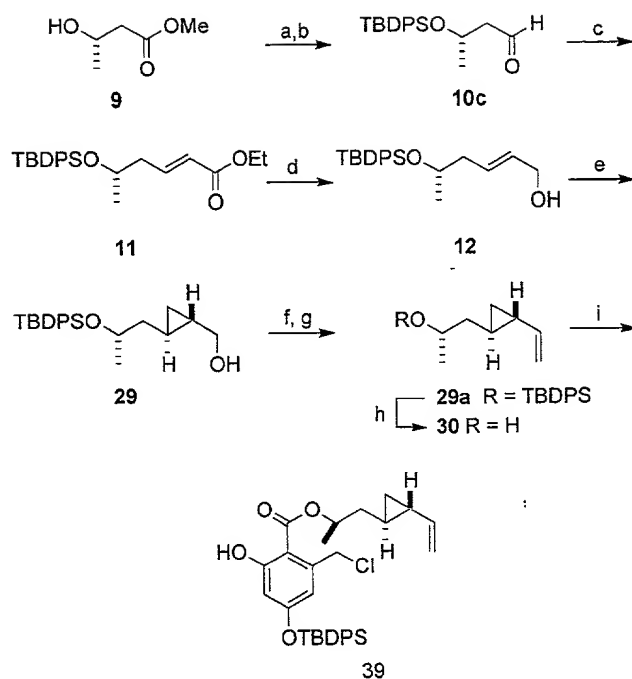


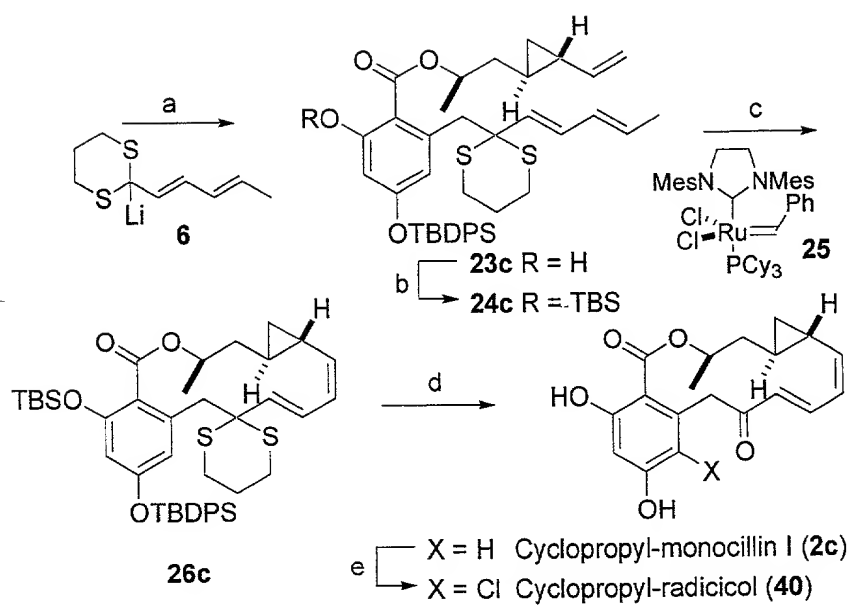
Figure 12

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^a (a) TBDPSCl, imid., >95%; (b) DIBAL-H, -78 °C, 92%; (c) LiCl, DIPEA (EtO)₂P(O)CH₂CO₂Et, 95%; (d) DIBAL-H, -20 °C, 96%; (e) (+)-tetramethyltartaric acid diamide-BBu, Et₂Zn, CH₂I₂, 9 >95% ee; (f) SO₃·pyridine, Et₃N, DMSO, 90%; (g) Ph₃PCH NaHMDS, 0 °C, 82%; (h) TBAF, 89%; (i) 7, P(furyl)₃, DIA benzene, 60%

Figure 13



a. *n*-BuLi, -78° C, 75% (3:1); b. TBSCl, 83%; c. 42 °C, 20%; d. (i) mCPBA, (ii) Ac₂O, Et₃N, H₂O, 60°C, (iii) NaHCO₃, MeOH, 60%; e. SO₂Cl₂, 80%

Figure 14

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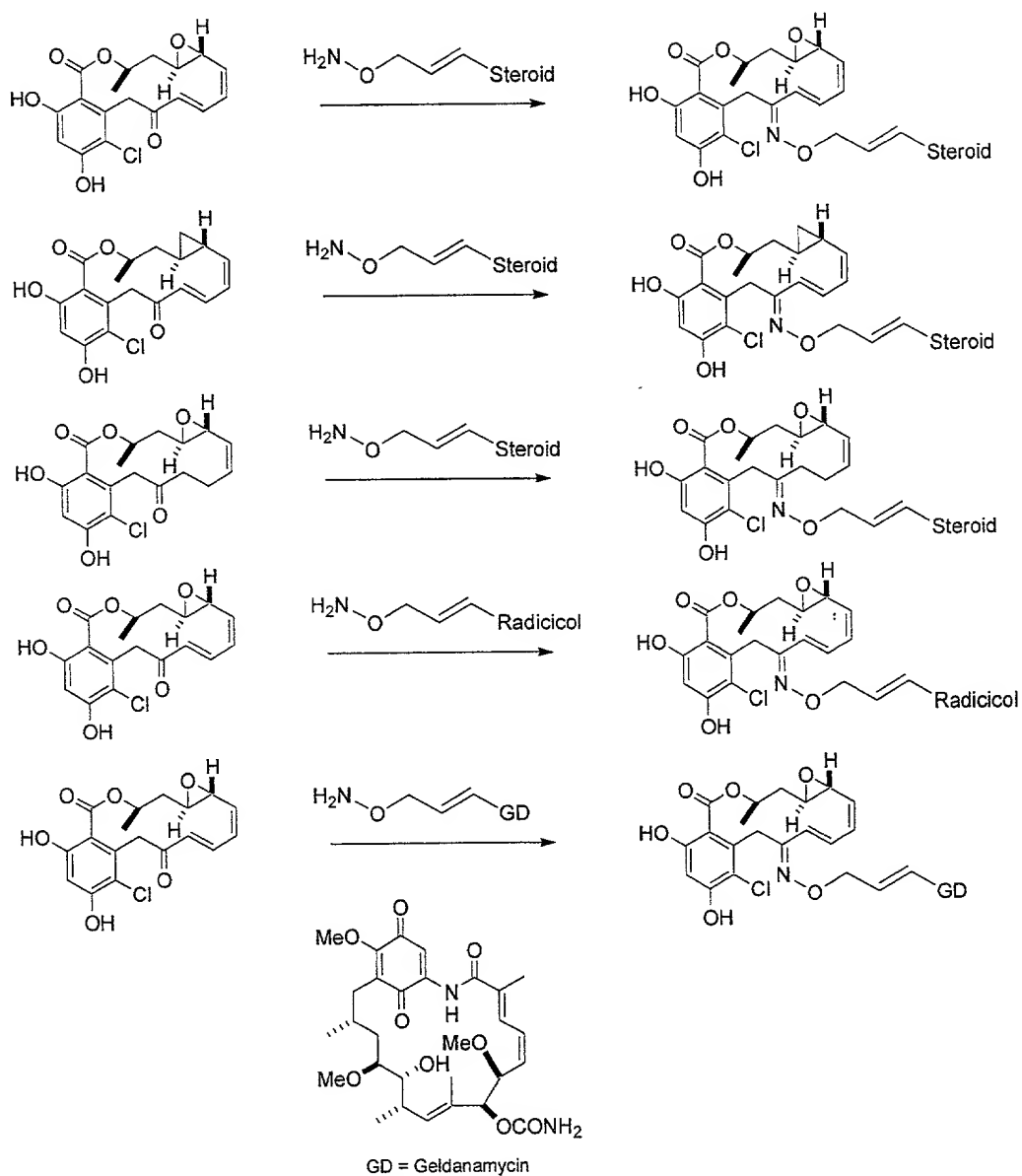


Figure 15

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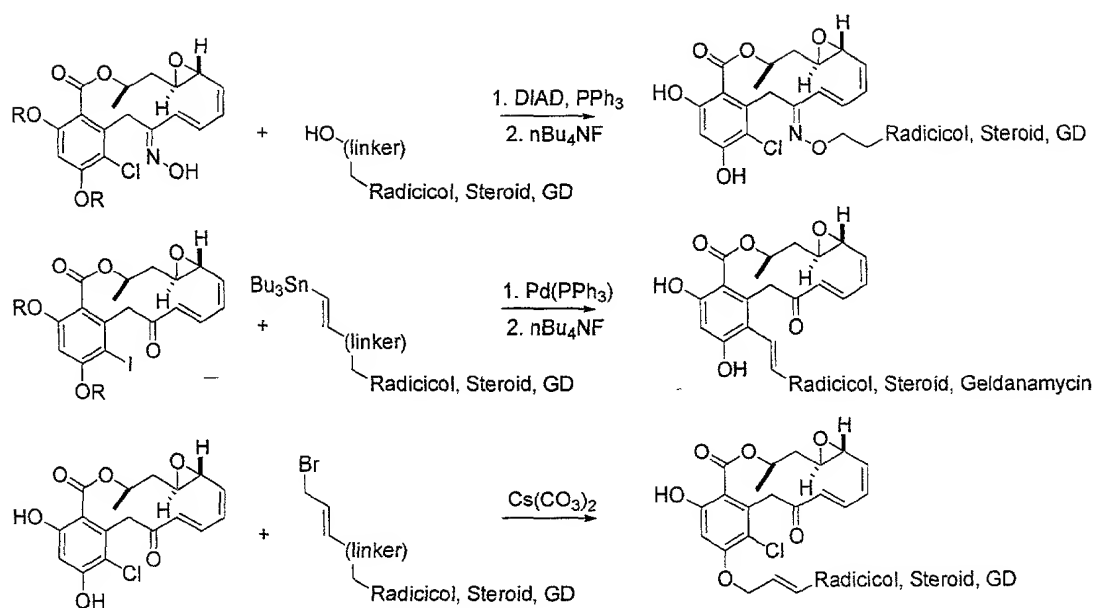
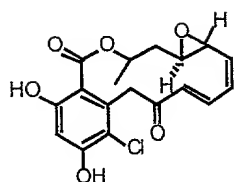


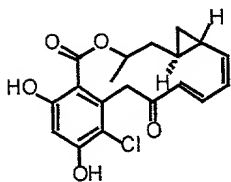
Figure 16

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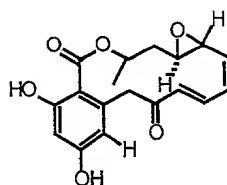
I. Radicicol



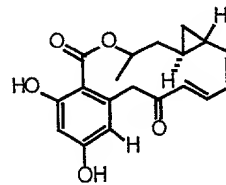
III. Cyclopropyl radicicol



II. Monocillin I



IV: Cyclopropyl monocillin



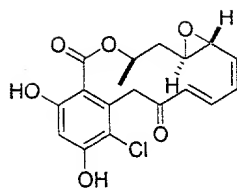
MCF7 Cells Treated with Radicicol and Analogues

vehicle radicicol cyclopropyl
0.5 1 2.5 5 0.5 1 2.5 5 μ M

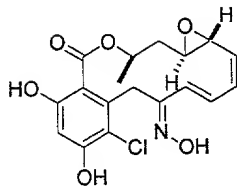
vehicle monocillin deschloro-cyclopropyl
0.5 1 2.5 5 0.5 1 2.5 5 μ M

KE R2

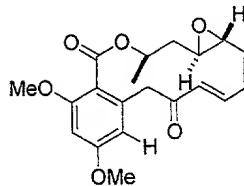
I. Radicicol



VII. Radicicol Oxime



V. Dimethyl Monocillin I



VI. Dimethyl Radicicol

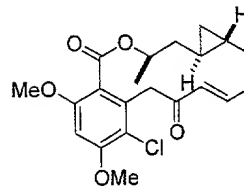
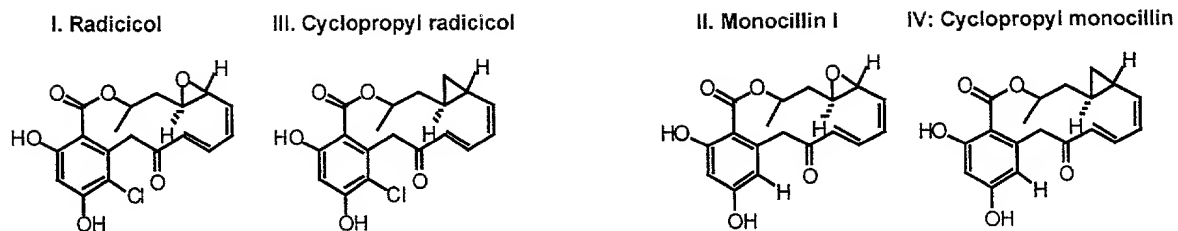


Figure 17

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BT474 Cells Treated with Novel Radicols (24 hrs.)

T042001/23550

vehicle	<u>radicicol</u>	<u>cyclopropyl</u>
0.5	1 2.5 5	0.5 1 2.5 5 μ M

vehicle	<u>monocillin</u>	<u>deschloro</u>
0.5	1 2.5 5	0.5 1 2.5 5 μ M

K&B2

Figure 18

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Growth of MCF7 Treated with Radicicol and Derivatives of Radicicol

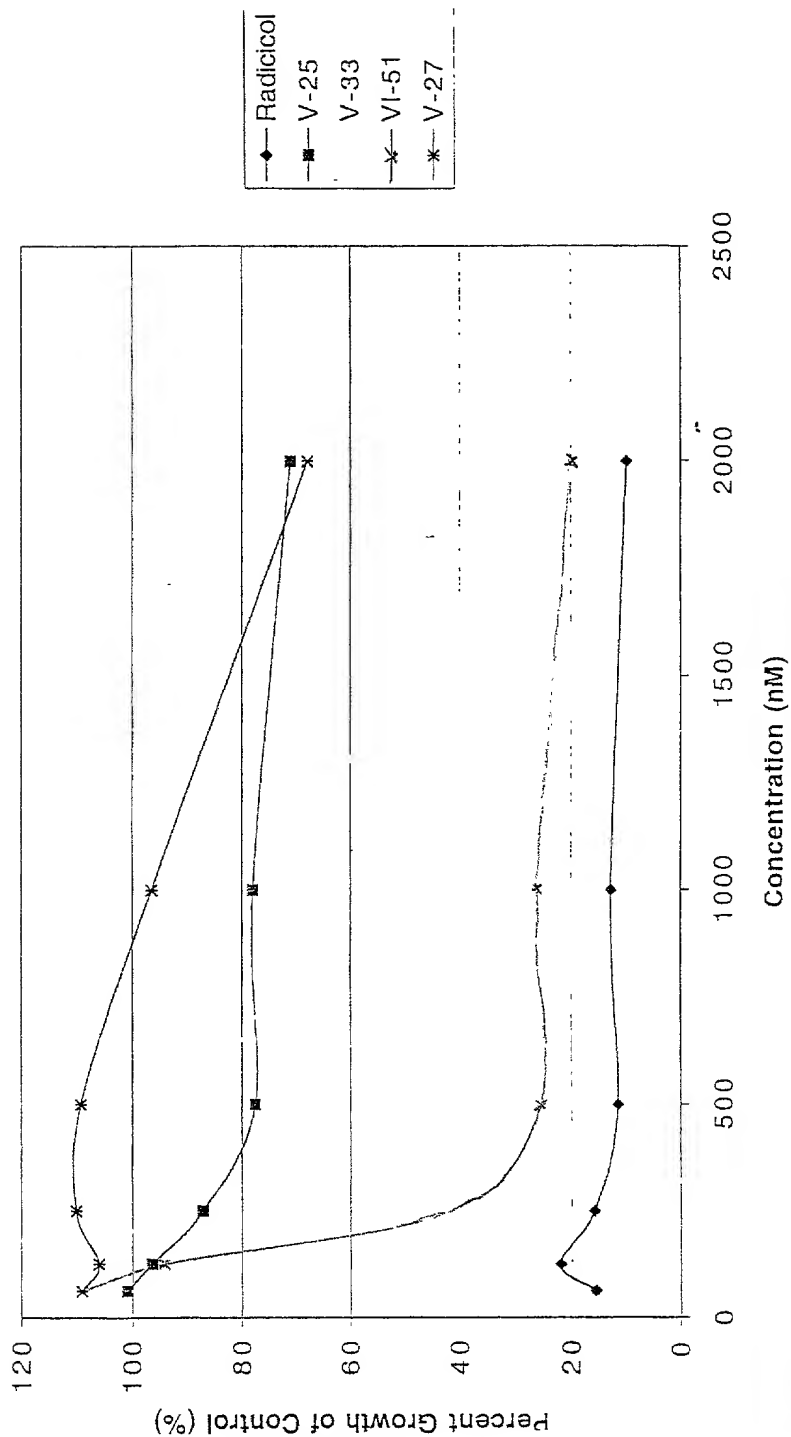


Figure 19

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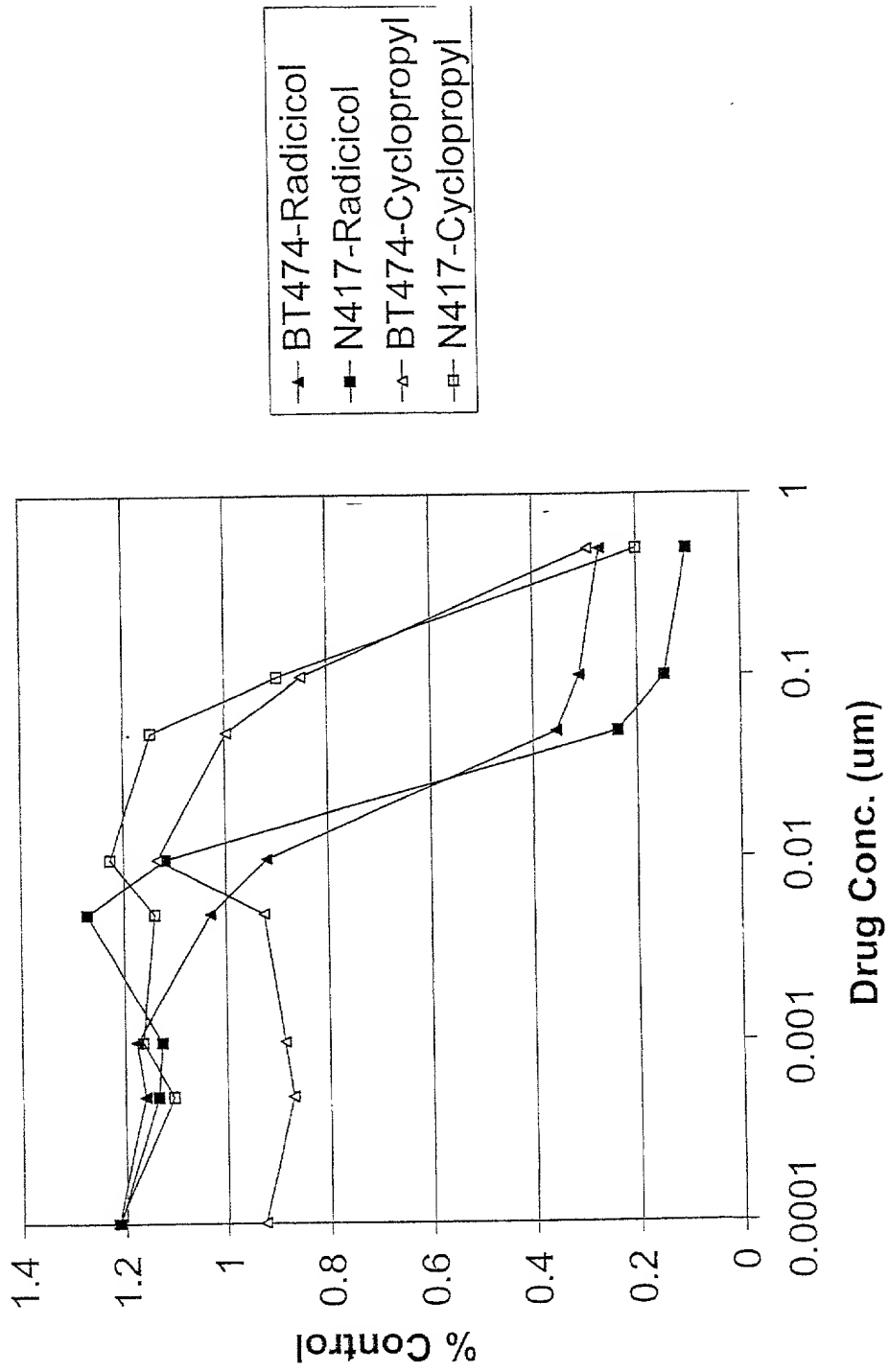


Figure 20

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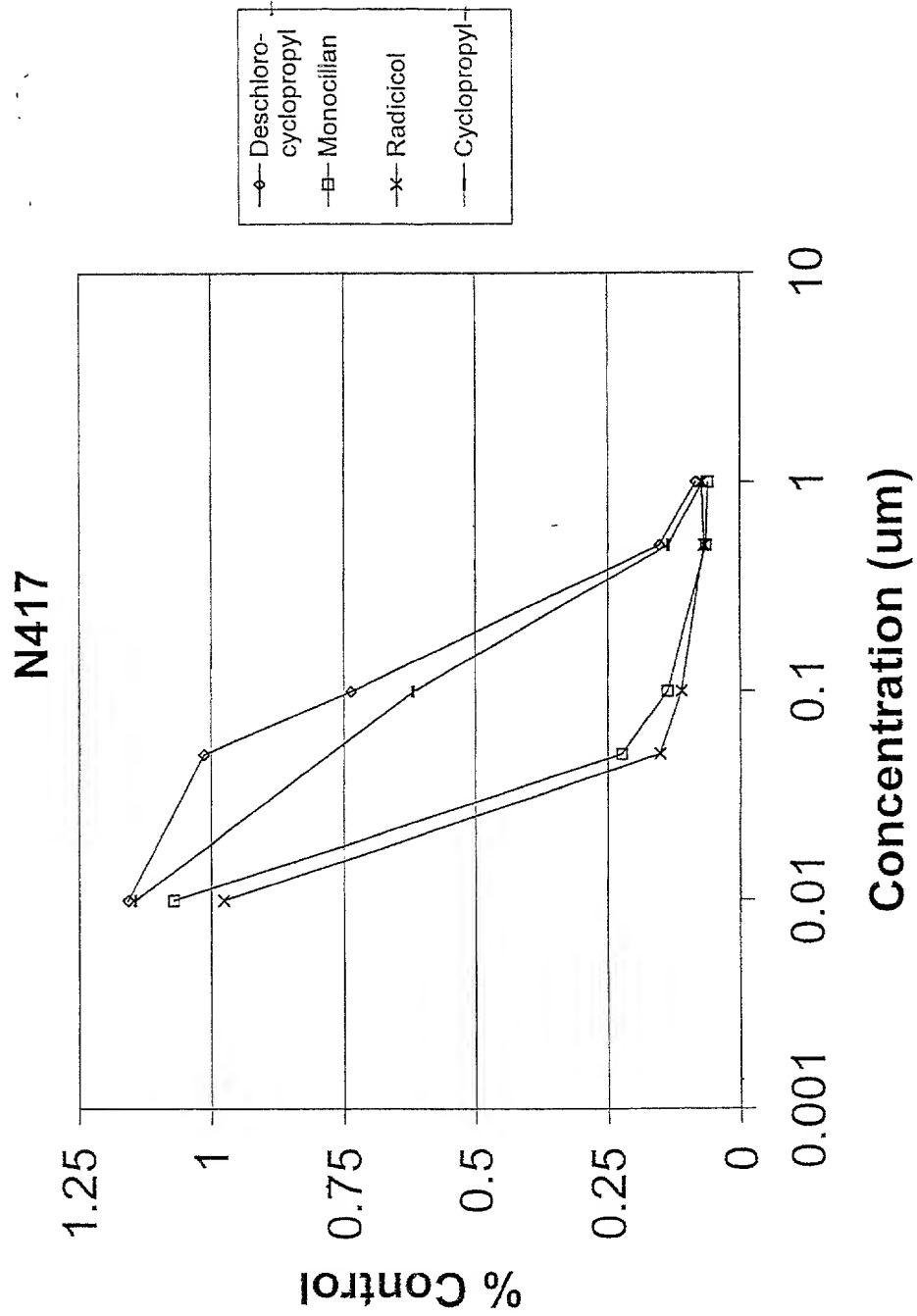


Figure 21